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Primary malignant melanoma of the esophagogastric junction: Report of a case

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ABSTRACT

INTRODUCTION: Primary malignant melanoma of the gastrointestinal tract is very rare, especially in the stomach. We report an extremely rare case of primary malignant melanoma of the esophagogastric junction mainly situated in the stomach.
PRESENTATION OF CASE: The patient was a 72-year-old woman who complained of shortness of breath due to severe anemia. Upper endoscopy revealed a soft easy-bleeding polypoid tumor just adjacent to the esophagogastric junction in the stomach. Biopsy of the tumor did not indicate a definite result, except malignant tumor. We performed total gastrectomy with splenectomy, and histological and immunohistological examination revealed malignant melanoma of the esophagogastric junction. She had no remote metastasis or lymphnodal metastasis at the point of surgery; however, she died of multiple metastases 11 months after the operation.
DISCUSSION: A definite preoperative diagnosis of primary malignant melanoma was very difficult to make from the preoperative biopsy specimen. This present case was first misinterpreted as undifferentiated carcinoma, or malignant lymphoma. Following the diagnosis of malignant melanoma, the question arose as to whether this was primary or metastatic (as malignant melanoma from other sites is known to metastasize to the stomach). Finally this tumor was diagnosed as a primary one due to the pathologic characteristics such as the existence of junctional activities.
CONCLUSION: We report an extremely rare case of primary malignant melanoma of the esophagogastric junction present in the stomach.
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1. Introduction

Malignant melanoma is a tumor with highly malignant potential. Though the majority of the malignant melanomas arise in the skin, other less common sites include the squamous mucous membranes such as the esophagus, eyes, and leptomeninges. Primary malignant melanoma of the esophagus is an extremely rare disease comprising approximately 0.1–0.2% of all esophageal malignancies.[1] Since biopsy specimens taken from the tumor often fails to identify the presence of malignant melanoma, preoperative definite diagnosis of this tumor is fairly difficult.

We herein present a rare case of primary malignant melanoma of the esophagogastric junction situated in the stomach and also discuss the difficulties in diagnosing this disease.

2. Presentation of case

A 72-year-old woman was admitted to our hospital due to shortness of breath on effort. Her past and family history was unremarkable. She did not complain of digestive symptoms, such as nausea or abdominal pain. Physical examination revealed marked anemia of the conjunctiva, but the nutritional status was not poor. Blood cell counts showed severe anemia, with a hemoglobin concentration of 4.2 g/dl. Tumor markers, CEA and CA19-9 especially, were within the normal range. Endoscopic examination showed a large easy-bleeding polypoid tumor just adjacent to the esophagogastric junction in the upper stomach (Fig. 1). Biopsy specimens taken twice from the tumor failed to identify the presence of malignant melanoma, suggesting it to be undifferentiated carcinoma or malignant lymphoma.

Upper GI examination using barium contrast showed a large polypoid tumor in the upper stomach just beside the esophagogastric junction (Fig. 2). Deformity of the stomach wall was too slight to suspect gastric cancer. Contrast-enhanced CT (CE-CT) showed a vascular-rich mass on the lesser curvature of the upper stomach (Fig. 3). The extent of wall invasion was diagnosed as the muscle

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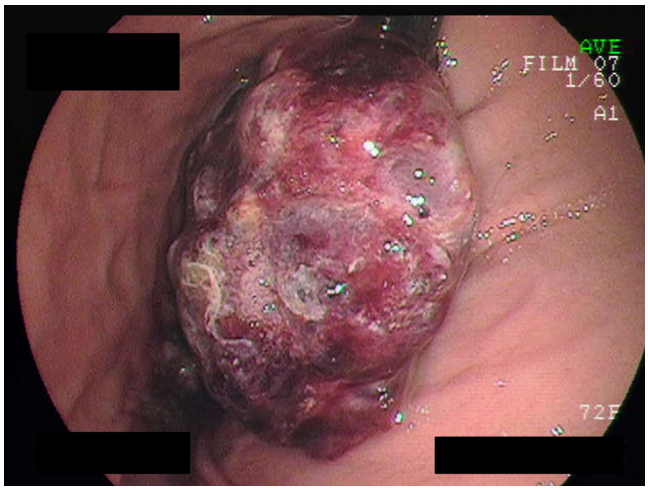


Fig. 1. Endoscopic examination showed a large easy-bleeding polypoid tumor just adjacent to the esophagogastric junction in the upper stomach.

layer of the stomach. There was no apparent lymphnodal swelling or liver metastasis on CE-CT.

Since the tumor was bleeding markedly, we decided to operate without a diagnosis. Total gastrectomy with splenectomy was performed, including D2 lymph node resection. The tumor was situated on the lesser curvature of the upper stomach, as shown by other investigations. No ascites or dissemination of the tumor was observed in the peritoneal cavity. Frozen sections of the esophageal excision stump revealed no malignant tumor cells. Reconstruction was performed with the usual R-Y method.

The resected specimen revealed a polypoid tumor, 6.7 cm × 8.1 cm in size, with partial black pigmentation, situated in the upper stomach (Fig. 4). The oral side of the tumor was barely attached to the esophageal mucosa. Histological examination of the specimen showed large nests of anaplastic, polymorphous tumor cells. At first, the dark, brown pigmentation was not noticed. The tumor invasion reached the muscles propria,

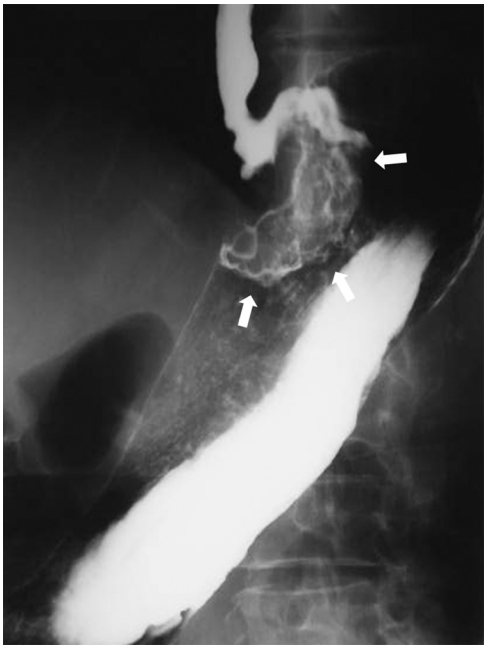


Fig. 2. Upper GI examination using barium contrast showed a large polypoid tumor in the upper stomach just beside the esophagogastric junction (arrows). No stenosis of the esophagogastric junction was observed.

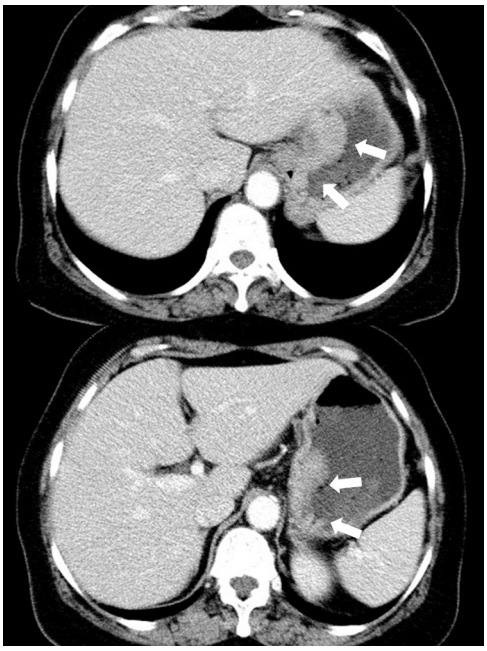


Fig. 3. CE-CT showed a vascular-rich mass on the lesser curvature of the upper stomach (arrows). No lymph nodal swelling or liver metastasis was noted.

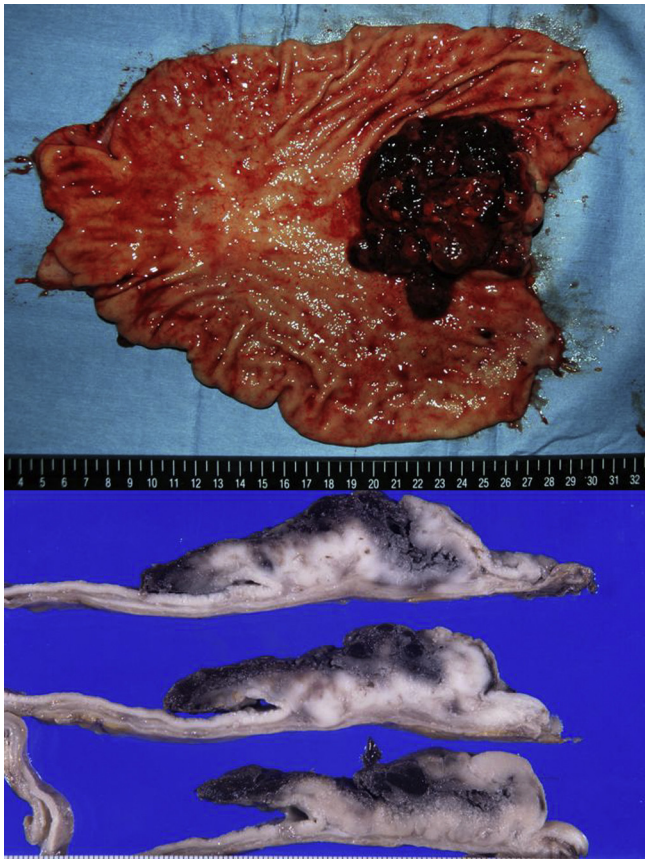


Fig. 4. Resected specimen of the whole stomach revealed a polypoid tumor, 6.7 cm × 8.1 cm in size, with partial black pigmentation, situated in the upper stomach. The tumor is scarcely attached to the esophageal mucosa.

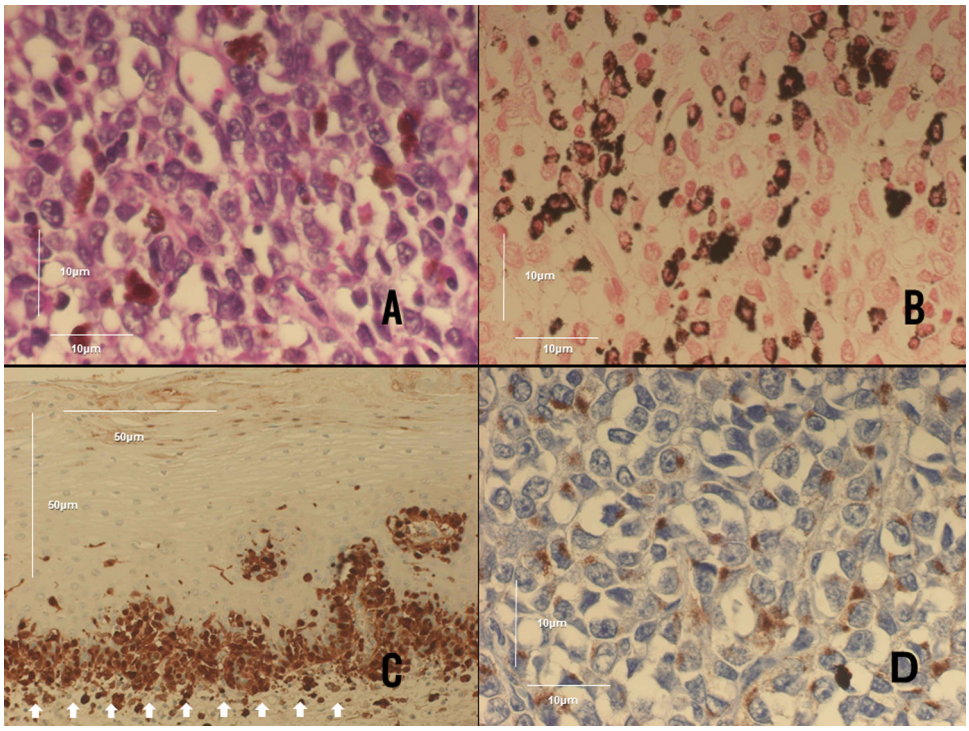
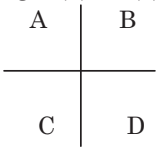


Fig. 5. (A) H&E, (B) Masson-Fontana, (C) S-100, and (D) HMB-45.



Immunohistological studies, such as S-100 protein(+) and HMB-45(+), confirmed the diagnosis of malignant melanoma. Junctional activities of atypical melanocytes with S-100 stain were observed (arrows).

with lymphatic invasion without vascular invasion. No lymph nodal metastasis was found in the stomach regional lymph nodes. Since the histological diagnosis was obscure, immunohistological studies were carried out and showed Fontana-Masson stain positive, HMB45 positive, S-100 protein positive. In addition, EMA negative, cytokeratin20 negative, and cytokeratin7 negative led us to the diagnosis of malignant melanoma. Close pathological examination of the mucosa of the distal end of the esophagus revealed the junctional activities of atypical melanocytes (Fig. 5).

Post-operatively, further examinations were performed to assess whether the tumor was metastasis or a primary tumor. Examination of the whole body skin was performed by a dermatologist, but revealed no pigmented region of the skin, and the retinas on both sides were examined by an ophthalmologist, but no suspicious primary lesion was found. PET (positron emission tomography)–CT was carried out to find other tumors which were the original focus or other metastases, but no hot spot was detected. These results implied a final diagnosis of primary malignant melanoma of the esophagogastric junction.

Systemic adjuvant chemotherapy was offered due to the aggressive potential of malignant melanoma, but the patient declined. The post-operative course was smooth for the first 3 months. CE-CT after 3 months showed no remote metastasis or any abnormal findings; however, 5 months after the operation, the patient was admitted because of left back pain, and CE-CT revealed metastatic tumor of malignant melanoma of the left adrenal gland with a bleeding mass around the left kidney as well as severe anemia. We were planning to operate immediately after admission, but as the pain from the bleeding mass stabilized, she rejected surgery.

Nine months after the operation, she developed left axillary lymph node metastases, and a subcutaneous metastatic tumor just right of the navel. At 10 months after the operation, metastatic tumors in the thoracic cavity and abdomen were newly found, she developed renal failure due to adrenal metastases, and died 11 months after the stomach operation.

3. Discussion

Malignant melanoma commonly originates from the skin and has a high grade of malignancy. It is rarely seen in the gastrointestinal tract, but primary esophageal and rectal malignant melanomas are reported sporadically. In particular, primary malignant melanoma of the esophagus is an extremely rare disease comprising approximately 0.1–0.2% of all esophageal malignancies.[1] In Japan, Yamaguchi reported a case of primary malignant melanoma and investigated 193 cases of primary malignant melanoma of the esophagus reported in Japan. According to his report, men predominated the cases by 2.2:1, with an overall mean age of 60.4 (21–89). The common symptoms were dysphagia (64.2%) and chest pain (9.3%), but 7.3% of the patients had no symptoms. The tumors were usually located in the middle and lower third of the esophagus (76.2%) and usually show a polypoid shape, and pigmentation.[2]

In our case, we observed no tumors in the esophagus lumen and the center of the tumor was in the upper stomach. Various differential diagnoses were considered beside malignant melanoma, because the tumor was found in the stomach. An accurate preoperative diagnosis of primary malignant melanoma was very difficult to make from the preoperative biopsy specimen which was first misinterpreted as undifferentiated carcinoma, or malignant lymphoma. Other authors have also referred to the difficulty of diagnosing preoperative biopsy specimens.[3,4]

After the operation, immunohistochemical examinations led us to the diagnosis. In particular, S-100 protein, HMB-45 and Vimentin were positive with cytokeratin negative, so we could make a definitive diagnosis.[5,6]

After the definite diagnosis of the malignant melanoma, the unique situation of the tumor made us wonder whether this tumor is primary or metastatic. Malignant melanoma in the stomach is usually metastatic, primary gastric malignant melanoma being extremely rare. A series of autopsies of patients with melanoma revealed gastric metastasis rates of more than 22%.[7] The diagnostic criteria for deciding whether the lesion is a primary or metastatic tumor were described by Raven and Dawson,[8] based on the proposals of Allen and Spitz.[9] They said that the tumor should have the structure of a melanoma, contain melanin granules and, most importantly, should arise from an area of junctional change within the squamous mucosa and that the adjacent epithelium should also show nests of atypical melanocytes with pleomorphic nuclei, called junctional changes; however if the tumor grows rapidly, sometimes the adjacent junctional changes might not be seen. Unfortunately this major criterion is met in only approximately 40% of cases.[10] If the major criterion is not met, other clinical factors, such as the absence of other primary sites of melanoma, and no history of removal of melanoma or an atypical melanocytic lesion from the skin or other organs should be significant.[11] However, as the pathology of this tumor showed junctional activities of atypical melanocytes in the mucosa of the distal esophagus, a definitive diagnosis of primary esophageal malignant melanoma was made. No history of skin or retinal melanoma, and a negative PET scan of the primary site confirmed this. As FDG-PET was reported to have the advantage of finding metastasis of malignant melanoma,[12] this information is strongly supportive of the primary melanoma.

Primary gastric malignant melanoma is extremely rare and only a few cases have been reported.[13,14] However, in our case, it is likely that the tumor arose from the esophageal mucosa of the esophagogastric junction given all the pathological findings, especially junctional activity. From all these considerations, we diagnosed this tumor as an extremely rare case of primary malignant melanoma of the esophagogastric junction which arose at the distal end of the esophagus and mainly extended into the stomach.

This is generally considered a highly malignant tumor which carries a poor prognosis with a rapidly fatal course. The present case died of the systemic spread of the disease only 11 months after surgery. Sabanathan et al. reported that the average overall survival of patients was 9.8 months and 5-year survival rate was only 1.69%.[1] But Volpin et al. reported the better 5-year survival rate as 37%.[15] Yamaguchi et al. reported the 5-year survival rate as 30% in a Japanese series in 2004. Their multivariate analysis with Cox's proportional hazard model showed that the most significant prognostic factor was the depth of tumor invasion.[2]

We regret that no adjuvant chemotherapy was given to the patient. Some researchers have mentioned the advantages of DAV (dacarbazin, nimustine, vincristine)[13] or immunotherapy,[14] but others found no effect against widespread metastasis and the poor prognosis of malignant melanoma.[3] Consequently, there are no definite adjuvant chemotherapies. While in the near future, effective systemic chemotherapy can be expected to further improve the survival rate.

4. Conclusion

We report an extremely rare case of malignant melanoma of the esophagogastric junction situated in the stomach, and suggest that doctors should be aware that malignant melanoma (whether primary or secondary) can occur in the gastro-intestinal tract. Given its poor prognosis, there is a need for more effective multimodal therapy.

Conflict of interest statement

None.

Funding

None.

Ethical approval

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Authors' contributions

Ishizaki M. who is the corresponding author was in charge of surgery of this patient and wrote this manuscript, Aibara Y. was in charge of diagnosing this patient, such as endoscopy, and PET CT, and Furuya K. took part in the pathological diagnosis of this patient.

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